reasonably convey to the skilled artisan that applicants had possession of the claimed invention at the time the application was filed. The Examiner contends that the appropriate inquiry is whether applicants have described the phenotypic consequences of altering the genotype. The Examiner contends that the phenotype of a transgenic animal remains unpredictable, and that applicants' embodiments are not representative of the products claimed.

Applicants traverse the rejection. Applicants submit that the Examiner's inquiry into whether applicants have described the phenotypic consequences of altering the genotype is not the appropriate inquiry. The test for sufficiency of support in a application is whether the disclosure reasonably conveys to the skilled artisan that the inventor had possession of the claimed subject matter at the time of filing. *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985). It does not matter how applicants convey the invention to one skilled in the art. *In re Wright*, 866 F.2d 422, 424, 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989). Therefore, contrary to the Examiner's assertions, applicants need not describe the phenotype of applicants' mice. Rather, a description of their genotype is sufficient if it reasonably conveys to the skilled artisan that applicants had possession of the claimed subject matter at the time of filing. *See Ralston Purina*, 227 U.S.P.Q. at 179. In this instance, applicants' description of the genotype of the mice is a sufficient description.

For example, the mere presence of a Group I endonuclease recognition site is all that is required of applicants' transgenic mice comprising a Group I endonuclease recognition site. The Group I endonuclease recognition site itself does not "express" anything. Furthermore, having read applicants' specification, the skilled artisan expects that the insertion of a Group I endonuclease recognition site in mice is a predictable

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

event. Applicants' description of the genotype of these mice in the specification reasonably conveys to the skilled artisan that applicants had possession of the claimed mice at the time of filing. Therefore, applicants' description is sufficient to fulfill 35 U.S.C. § 112, first paragraph.

Similarly, although applicants' claimed invention encompasses mice in which a Group I endonuclease is expressed, the mere presence of a nucleotide sequence encoding a Group I endonuclease is all that is required of applicants' transgenic mice comprising a nucleotide sequence encoding a Group I endonuclease. For example, when linked to an inducible promoter, the nucleotide sequence encoding a Group I endonuclease may not "express" anything until it is induced. Furthermore, having read applicants' specification, the skilled artisan expects that the insertion of a nucleotide sequence encoding a Group I endonuclease in mice is a predictable event. Again, applicants' description of the genotype of these mice in the specification reasonably conveys to the skilled artisan that applicants had possession of the claimed mice at the time of filing.

Applicants described representative Group I endonuclease recognition sites and Group I endonucleases on pages 26-27 and in Figure 6 of the specification. For example, applicants described multiple examples of Class I endonucleases, which is the largest family of Group I endonucleases, and one example each of Class II-V endonucleases, which are much smaller families of Group I endonucleases. The Examiner has not given any reasons why the listed endonucleases are not representative of the claimed endonucleases. Accordingly, applicants respectfully request withdrawal of the rejection.

Moreover, applicants' described the insertion of a representative species of Group I endonuclease recognition site, I-*Sce*I, into mouse D3 cells. (Specification at 38.) Applicants' working example is representative of the insertion of any and all Group I

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

endonuclease recognition sites. Accordingly, there can be no doubt that applicants' had possession of mice comprising any and all Group I endonuclease recognition sites.

With respect to the adequate description of a genus, the Federal Circuit has stated:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by the nucleotide sequence, falling within the scope of the genus . . . .

University of *California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568, 43 U.S.P.Q. 2d 1398, 1406 (Fed. Cir. 1997). Applicants have provided nucleotide sequences of a representative number of Group I endonuclease recognition sites, which will work in the claimed invention. Consequently, the requirements of the 35 U.S.C. § 112, first paragraph, have been fulfilled. *See id.* Accordingly, applicants respectfully request withdrawal of the rejection.

Claims 48-93 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to enable the skilled artisan to make and/or use the invention. The Examiner contends that the phenotype of a transgenic animal is determined by a complex interaction of genetics and environment, and that it is difficult to predict the behavior of a transgene in any and all animals. The Examiner further contends that the specification fails to disclose that implantation of any selected clone leads to the making of a transgenic mouse. It is the Examiner's position that it is unclear how the skilled artisan would use D3 embryonic stem cells without an excessive and undue amount of experimentation to generate transgenic mice encoding any and all Group-I intron encoded endonuclease sites. The Examiner conceded that the skilled artisan would have been able to make the required genetic constructs encoding any and all Group I encoded endonuclease sites. However, the Examiner concludes: "It is unclear how one skill[ed] in the art would exercise the

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

invention as claimed when the phenotype of a transgenic mouse (as required) is not known." (Paper No. 15 at 8.)

Applicants traverse the rejection. As discussed above, the ***genotype*** of applicants' mice is predictable. Furthermore, as previously detailed in the Amendment and Response filed December 4, 2000, no undue experimentation would be required to practice the claimed invention. As evidence of this fact, the D3 cells described in the specification were actually used to generate transgenic mice containing I-*Sce*I sites. Applicants have enclosed a Declaration of Andre Choulika attesting to the creation of transgenic mice from the D3 cells in the specification. The amount of experimentation required was no more than routine screening. Accordingly, applicants submit that the claimed invention is fully enabled and respectfully request withdrawal of the rejection.

Applicants respectfully submit that this application is now in condition for allowance. In the event that the Examiner disagrees, he is invited to call the undersigned to discuss any outstanding issues remaining in this application in order to expedite prosecution.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____

Salvatore J. Arrigo
Reg. No. 46,063
Tel: 202-408-4000
Fax: 202-408-4400
E-mail: salvatore.arrigo@finnegan.com

Dated: October 10, 2001

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000